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EXAMINER	
ANDERSON, JAMES D	

ART UNIT	PAPER NUMBER
1614	

NOTIFICATION DATE	DELIVERY MODE
07/10/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/758,335	ORLOW ET AL.	
	Examiner	Art Unit	
	James D. Anderson	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *47-49,51-56,60-62 and 64-69* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *47-49,51-55,60-62 and 64-68* is/are rejected.

7)☒ Claim(s) *56 and 69* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1 sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

CLAIMS 47-49, 51-56, 60-62 & 64-69 ARE PRESENTED FOR EXAMINATION

Applicants' amendment and Information Disclosure Statement filed 4/23/2007 have been received and entered into the application. Accordingly, claims 47, 56, 60 and 69 have been amended. Also, as reflected by the attached, completed copy of USPTO Form 1449 the cited references have been considered.

The amendments and Applicants' remarks have overcome the rejections not reiterated herein from the previous office action. Such rejections are hereby withdrawn. The following rejections are either reiterated or newly applied and constitute the totality of issues remaining in the present application.

In light of the new rejections being applied against the pending claims, this Office Action is **Non-Final**.

Response to Arguments

Applicants' arguments, see Response, filed 4/23/2007, with respect to the 35 U.S.C. § 112, 1st Paragraph (Enablement) rejection of claims 47-49, 51-56, 60-62 and 64-69 have been fully considered and are persuasive. The 35 U.S.C. § 112, 1st Paragraph (Enablement) rejection of claims 47-49, 51-56, 60-62 and 64-69 has been *withdrawn*.

Applicant's arguments and amendments, see Response, filed 4/23/2007, with respect to the 35 U.S.C. § 112, 2nd Paragraph rejection of claims 47-49, 51-56, 60-62 and 64-69 have been fully considered and are persuasive. The 35 U.S.C. § 112, 2nd Paragraph rejection of claims 47-49, 51-56, 60-62 and 64-69 has been *withdrawn*.

Applicant's amendments, see Response, filed 4/23/2007, with respect to the 35 U.S.C. § 102(b) rejection of claims 47 and 60 are sufficient to obviate the present rejection. Accordingly, the 35 U.S.C. § 102(b) rejection of claims 47 and 60 has been *withdrawn*.

With respect to the 35 U.S.C. § 102(b) rejections of claims 47-49, 51-52, 55, 60-62, 64-65 and 68, Applicant's arguments filed 4/23/2007 have been fully considered but they fail to persuade the Examiner of an error in his determination that the cited references inherently anticipate the present claims.

Firstly, with respect to U.S. Patent No. 5,616,332 (claims 47, 55, 60 and 68) Applicants argue that the reference does not teach all of the limitations of the instant claims. For example, Applicants argue that the concentrations of sphingosine disclosed in U.S. 5,616,332 may not be pharmaceutically effective amounts that effect an alteration in late endosomal/lysosomal trafficking and thus decrease melanogenesis as claimed. This argument is not persuasive for two reasons. First, the instant claims do not recite a limitation wherein the "effective amount" is an amount that effects an alteration in late endosomal/lysosomal trafficking. The claims only recite administration of an effective amount of a compound that effects an alteration in late endosomal/lysosomal trafficking. The fact that sphingosine is administered in U.S. 5,616,332 in amounts that reduce irritation from other components in the composition reads on "an effective amount". In fact, the reference teaches compositions comprising 0.001 to 5% by weight sphingosine. Second, there is nothing in the instant Application that would indicate exactly what amounts of sphingosine elicit the claimed activity. Accordingly, in the absence of evidence to the contrary, the Examiner maintains that topical application of a composition comprising an effective amount (0.001 to 5% by weight) of sphingosine as taught in U.S. 5,616,332 inherently

anticipates the instantly claimed methods. Applicants' discovery of a mechanism of action or another beneficial effect of such topical application does not render the instantly claimed methods patentable over those taught in U.S. 5,616,332.

Secondly, with respect to U.S. Patent No. 5,569,678 (claims 47, 49, 51-52, 60, 62 and 64-65) Applicants argue that practicing the methods of U.S. 5,569,678 would not necessarily result in carrying out Applicants' claimed invention. For example, Applicants argue that applying trifluoperazine to wounds or scars is distinct from skin. This argument is not persuasive because U.S. 5,569,678 explicitly recites topically administering a composition comprising a calcium channel antagonist (*e.g.*, trifluoperazine) to a wound or scar. Clearly, if such a wound or scar is present on the skin the methods of U.S. 5,569,679 read on the instant claims. Applicants' discovery of a mechanism or another beneficial effect of such topical application does not render the instantly claimed methods patentable over those taught in U.S. 5,569,679. The Examiner maintains that topical administration of trifluoperazine to a wound or scar reads on the instantly claimed methods.

Thirdly, with respect to U.S. Patent No. 4,439,432 (claims 47-48 and 60-61) Applicants argue that the reference does not necessarily possess the characteristics of Applicants' claimed methods. Applicants argue that U.S. 4,439,432 gives no indication that the progesterone in the disclosed composition is present "in pharmaceutically effective amounts" or is properly formulated to effect an alteration in late endosomal/lysosomal trafficking. This argument is not persuasive for the same reasons Applicants' arguments traversing the rejection with respect to U.S. 5,616,332 are not persuasive. U.S. 4,439,432 teaches compositions of a "high concentration" solution of progesterone that can be used transdermally for the correction of

progesterone deficiency. Amounts of 1 to 25% progesterone by weight are taught (col. 2, lines 45-50) and the resulting emulsion is "applied to the skin" (col. 2, lines 67-68). Accordingly, in the absence of a showing to the contrary, the Examiner maintains that a formulation comprising 1 to 25% progesterone that is topically applied to the skin reads on the instantly claimed methods. Applicants' discovery of a mechanism or another beneficial effect of such topical application does not render the instantly claimed methods patentable over those taught in U.S. 4,439,432.

The rejections of claims 47-49, 51-52, 55, 60-62, 64-65 and 68 are maintained for the reasons of record and reiterated below.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 47, 55, 60 and 68 are rejected under 35 U.S.C. § 102(b) as being anticipated by Herstein (U.S. Patent No. 5,616,332; Issued Apr. 1, 1997).

The instant claims recite a method of decreasing melanin production in a melanocyte (claims 47 and 55) and a method of reducing skin pigmentation (claims 60 and 68) comprising administering an effective amount of sphingosine. It is noted that both methods would ideally call for topical administration of sphingosine.

Herstein teaches a cosmetic skin-renewal composition comprising sphingosine (Abstract). The topical administration of sphingosine is taught to reduce long-term irritation induced by topical application of skin-renewal stimulating acids to the skin (col. 2, lines 10-13). The preparations taught in Herstein can be used on any skin area and can be helpful in alleviating problems of wrinkles, sun damage and cracking with some effect on age spots (col. 18, lines 63-67). Claim 1 of the Herstein patent recites a method comprising administering a sphingosine-containing composition that is applied by topical application daily. The reference thus teaches the topical application of a sphingosine-containing composition. As such, decreasing melanin production in a melanocyte and reducing skin pigmentation would inherently result from said topical application.

It is noted that *In re Best* (195 USPQ 430) and *In re Fitzgerald* (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter, which there is reason to believe inherently includes functions that are newly cited, or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to "prove that subject matter to be shown in the prior art does not possess the characteristic relied on" (205 USPQ 594, second column, first full paragraph). There is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of invention, but only that the subject matter is in fact inherent in the prior art reference. *Schering Corp. v. Geneva Pharm. Inc.*, 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003); see also *Toro Co. v. Deere & Co.*, 355 F.3d 1313, 1320, 69 USPQ2d 1584, 1590 (Fed. Cir. 2004) ("[T]he fact that a characteristic is a necessary feature or result of a prior-art embodiment (that is itself sufficiently described and

enabled) is enough for inherent anticipation, even if that fact was unknown at the time of the prior invention").

In the instant case, the topical application of sphingosine will necessarily result in decreasing melanin production in a melanocyte and reducing skin pigmentation.

Claims 47, 49, 51-52, 60, 62 and 64-65 are rejected under 35 U.S.C. § 102(b) as being anticipated by Lee (U.S. Patent No. 5,569,678; Issued Oct. 29, 1996).

The instant claims recite a method of decreasing melanin production in a melanocyte (claims 47, 49 and 51-52) and a method of reducing skin pigmentation (claims 60, 62 and 64-65) comprising administering an effective amount of a phenothiazine. It is noted that both methods would ideally call for topical administration of a phenothiazine.

Lee teaches a method of controlling wound scar production by administering a calcium antagonist to the wound site (Abstract). The reference teaches that the calcium antagonist can be a calmodulin inhibitor such as trifluorperazine (col. 3, lines 41-43 and 47-49). The calcium antagonists are preferably administered by topical application to the wound site (col. 5, lines 36-39). Lee claims a method of controlling scar production comprising administering an effective amount of a calcium antagonist (claim 1), including the topical administration of trifluoperazine (claims 5 and 6). The reference thus teaches the topical application of trifluoperazine. As such, decreasing melanin production in a melanocyte and reducing skin pigmentation would inherently result from said topical application.

It is noted that *In re Best* (195 USPQ 430) and *In re Fitzgerald* (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter, which there is reason to

believe inherently includes functions that are newly cited, or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to "prove that subject matter to be shown in the prior art does not possess the characteristic relied on" (205 USPQ 594, second column, first full paragraph). There is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of invention, but only that the subject matter is in fact inherent in the prior art reference. *Schering Corp. v. Geneva Pharm. Inc.*, 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003); see also *Toro Co. v. Deere & Co.*, 355 F.3d 1313, 1320, 69 USPQ2d 1584, 1590 (Fed. Cir. 2004) ("[T]he fact that a characteristic is a necessary feature or result of a prior-art embodiment (that is itself sufficiently described and enabled) is enough for inherent anticipation, even if that fact was unknown at the time of the prior invention").

In the instant case, the topical application of trifluoperazine will necessarily result in decreasing melanin production in a melanocyte and reducing skin pigmentation.

Claims 47-48 and 60-61 are rejected under 35 U.S.C. § 102(b) as being anticipated by Peat (U.S. Patent No. 4,439,432; Issued Mar. 27, 1984).

The instant claims recite a method of decreasing melanin production in a melanocyte (claims 47-48) and a method of reducing skin pigmentation (claims 60-61) comprising administering an effective amount of progesterone. It is noted that both methods would ideally call for topical administration of progesterone.

Peat teaches compositions and methods for the correction of progesterone deficiency comprising the transdermal, oral or suppository administration of a high concentration solution

of progesterone (Abstract). Progesterone is taught to be useful in treating psoriasis, eczema, and senile skin changes including warts and superficial burns (col. 1, lines 46-56). The compositions taught in Peat can be administered by spreading on the skin (col. 2, lines 15-22). Peat claims a method of administering progesterone to a patient in need thereof comprising administering progesterone "by means other than intravenous injection" (claim 5), including topical administration (claim 7). The reference thus teaches the topical application of progesterone to a patient in need thereof. As such, decreasing melanin production in a melanocyte and reducing skin pigmentation would inherently result from said topical application.

It is noted that *In re Best* (195 USPQ 430) and *In re Fitzgerald* (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter, which there is reason to believe inherently includes functions that are newly cited, or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to "prove that subject matter to be shown in the prior art does not possess the characteristic relied on" (205 USPQ 594, second column, first full paragraph). There is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of invention, but only that the subject matter is in fact inherent in the prior art reference. *Schering Corp. v. Geneva Pharm. Inc.*, 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003); see also *Toro Co. v. Deere & Co.*, 355 F.3d 1313, 1320, 69 USPQ2d 1584, 1590 (Fed. Cir. 2004) ("[T]he fact that a characteristic is a necessary feature or result of a prior-art embodiment (that is itself sufficiently described and enabled) is enough for inherent anticipation, even if that fact was unknown at the time of the prior invention").

In the instant case, the topical application of progesterone will necessarily result in decreasing melanin production in a melanocyte and reducing skin pigmentation.

New Grounds of Rejection

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 53 and 66 are rejected under 35 U.S.C. § 102(e) as being anticipated by Frome (U.S. Patent No. 6,197,830; Issued Mar. 6, 2001; Filed Sep. 22, 1995).

Instant claims 53 and 66 recite methods of decreasing melanin production (claim 53) and reducing skin pigmentation (claim 66) comprising administering a tricyclic antidepressant.

Frome teaches methods of achieving pain relief comprising topical application of compositions comprising tricyclic antidepressants (Abstract; col. 3, line 47 to col. 4, line 32). Specifically, Frome exemplifies a topical composition comprising 0.05% amitriptylline (col. 5, lines 10-21). Such a composition is topically applied to the skin to effect pain relief (*id.* at lines 41-55). It is the Examiner's position that topical application of a 0.05% amitriptylline composition to the skin inherently reads on the instantly claimed methods. It is noted that *In re Best* (195 USPQ 430) and *In re Fitzgerald* (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter, which there is reason to believe inherently includes

functions that are newly cited, or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to "prove that subject matter to be shown in the prior art does not possess the characteristic relied on" (205 USPQ 594, second column, first full paragraph). There is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of invention, but only that the subject matter is in fact inherent in the prior art reference. *Schering Corp. v. Geneva Pharm. Inc.*, 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003); see also *Toro Co. v. Deere & Co.*, 355 F.3d 1313, 1320, 69 USPQ2d 1584, 1590 (Fed. Cir. 2004) ("[T]he fact that a characteristic is a necessary feature or result of a prior-art embodiment (that is itself sufficiently described and enabled) is enough for inherent anticipation, even if that fact was unknown at the time of the prior invention"). In the instant case, while Frome does not disclose that topical application of 0.05% amitriptylline results in reduced skin pigmentation or decreased melanin production, such functions are an inherent result of such administration. As such, Applicants' claims, which recite no specific doses required to elicit the claimed effects, are inherently anticipated by the topical application of 0.05% amitriptylline to the skin.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. § 103(c) and potential 35 U.S.C. § 102(e), (f) or (g) prior art under 35 U.S.C. § 103(a).

Claims 54 and 67 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Frome (U.S. Patent No. 6,197,830; Issued Mar. 6, 2001; Filed Sep. 22, 1995) in view of The Merck Index, 12th Edition (1996, Merck & Co., Inc., Whitehouse Station, N.J., pages 581, 845, 1154, 1358 and 1656).

Frome discloses as discussed *supra*. The reference does not disclose the tricyclic antidepressants as recited in instant claims 54 and 67.

However, The Merck Index discloses that the instantly claimed imipramine, nortryptyline, protryptyline, trimipramine and doxepin are antidepressants that all have a tricyclic structure. As such, the agents are reasonably classified as "tricyclic antidepressants" as disclosed as useful in the methods of Frome.

As such, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to topically administer any tricyclic antidepressant as broadly disclosed in Frome. The motivation to do so is found in Frome, who discloses methods of topically administering "tricyclic antidepressants" of which amitriptylline is provided as an example (col. 3, lines 62-65). The skilled artisan would have been imbued with at least a

reasonable expectation that topical application of the tricyclic antidepressants recited in The Merck Manual would be effective in the methods disclosed in Frome. As discussed *supra*, such topical administration will naturally result in the effects instantly claimed.

Allowable Subject Matter

Claims 56 and 69 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James D. Anderson whose telephone number is 571-272-9038. The examiner can normally be reached on MON-FRI 9:00 am - 5:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR

system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

James D. Anderson
Patent Examiner
AU 1614

July 2, 2007

Phyllis Spivack

PHYLLIS SPIVACK
PRIMARY EXAMINER

7/2/07